Antimicrobial resistance profile of bacteria isolated from infections and the ocular microbiota

Perfil de resistencia antimicrobiana de bacterias aisladas de infecciones y de la microbiota ocular

Laura Victoria Martín Algarra*✉
Martha Catalina Sánchez**
Geraldine Rondón Correa**
Martha Fabiola Rodríguez***

ABSTRACT

Introduction: The increase in strains resistant to antimicrobials in recent years may be due to their indiscriminate and excessive use. The World Health Organization (WHO) has promoted global surveillance of antimicrobial resistance; however, the biggest limitation is a lack of reliable data in some countries. Studies such as the Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR) (2009 and 2013) and the Tracking Resistance in the United States Today (TRUST) report that the most prevalent microorganism in infections worldwide is *Staphylococcus aureus*, with a high percentage of Methicillin-resistant *Staphylococcus aureus* (MRSA), which are of great importance for public health due to their high resistance to antimicrobials. *Objetive:* To identify the main antimicrobial resistance profiles of bacteria isolated from infections or from ocular microbiota. *Methods:* A systematic review of literature in EBSCOhost databases: Academic Search, Medline, ScienceDirect, Web of Science, Springer, PubMed, and Google Academics, with keywords such as *ocular, antimicrobial*, and *resistance*, between 2010 and 2017. *Results:* 30 articles on antimicrobial resistance from the last seven years were analyzed. In most countries, the genus *Staphylococcus* (*S. aureus*, 45%, NEC, 37%), *Pseudomonas* (8%) and *Streptococcus* (7%) were predominant. The lowest percentages were *Corynebacterium* (2%) and *Klebsiella* (1%). *Conclusions:* Most of the ocular isolates reported in the global context show resistance to beta-lactams. Increased resistance to these antibiotics implies a serious therapeutic problem in the hospital setting.

Keywords: bacteria, ocular globe, bacterial infections, microbiota, microbial resistance to antibiotics.

* Optometrist, Universidad de La Salle, Colombia. Cisvi Research Center. MA student in Vision Sciences. ✉ lmartin32@unisalle.edu.co
** Optometrist. Universidad de La Salle, Colombia.
*** Bacterologist. MSc. Professor. Cisvi Research Center, Universidad de La Salle, Colombia.

Martín Algarra LV, Sánchez MC, Rondón Correa G, Rodríguez MF

RESUMEN

En los últimos años, el aumento de cepas resistentes a los antimicrobianos puede deberse a su uso indiscriminado y excesivo. La Organización Mundial de la Salud (OMS) ha promovido la vigilancia mundial de la resistencia a los antimicrobianos; sin embargo, la mayor limitante es la falta de datos confiables en algunos países. Estudios como el Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR), de 2009 y 2013, y el Tracking Resistance in the United States Today (TRUST) refieren que el microorganismo más prevalente en infecciones en el mundo es el *Staphylococcus aureus* y un alto porcentaje son *Staphylococcus aureus* meticilino resistente (SAMR), que son de gran importancia para la salud pública por su alta resistencia a los antimicrobianos. *Objetivo:* identificar los principales perfiles de resistencia antimicrobiana de bacterias aisladas de infecciones o de la microbiota ocular. *Métodos:* revisión sistemática de la literatura en las bases de datos EBSCOhost: Academic Search, Medline, ScienceDirect, Web of Science, Springer, PubMed y Google Academic, con las palabras clave *ocular*, *antimicrobial* y *resistance*, entre 2010 y 2017. *Resultados:* se analizaron 30 artículos de los últimos siete años sobre resistencia antimicrobiana. En la mayoría de países predominó el género *Staphylococcus* (*S. aureus*, 45 %; ECN, 37 %), *Pseudomona* (8 %) y *Streptococcus* (7 %). Los porcentajes más bajos fueron de *Corynebacterium* (2 %) y *Klebsiella* (1 %). *Conclusiones:* la mayoría de los aislados del globo ocular reportados en el contexto mundial presentan resistencia a los betalactámicos. El incremento en la resistencia a estos antibióticos implica un grave problema terapéutico en el ámbito hospitalario.

Palabras clave: bacterias, globo ocular, infecciones bacterianas, microbiota, resistencia microbiana a antibióticos.

INTRODUCTION

Antimicrobial resistance is a natural phenomenon acquired through genetic recombination mechanisms proper to bacteria or through mutations. In recent years, the relative increase in resistant strains seems to have been due to an indiscriminate and excessive use of antimicrobials, which exert a selective pressure on these bacteria. Therefore, the emergence of antimicrobial resistance in a country is dependent on regulations, control plans, and infectious disease prevention (1). The World Health Organization (WHO), the Food and Drug Administration (FDA), and the Centers for Disease Control and Prevention in several countries (2-4) have promoted the global surveillance of antimicrobial resistance, in order to reduce its appearance and spread. However, in the 21st century, the biggest limitation is the lack of reliable data in some countries, mainly in Africa and Asia.

In the Americas, the Antimicrobial Resistance Surveillance Network for Latin America (ReLARA) and the Pan American Health Organization (PAHO) provide information on national reference laboratories of 19 countries in Latin America,

Canada, and the United States that are part of the network. In Europe, the European Antimicrobial Resistance Surveillance (EARS) includes the 28 countries of the European Union; Central and Eastern Europe count on the Central Asian and Eastern European Surveillance of Antimicrobial Resistance (CAESAR) network, the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), and the Dutch National Institute of Public Health and Environment (RIVM), which help to strengthen epidemiological studies and the capacity and quality of laboratories in the region. In the Southeast Asia region, there are no data collection organizations. Since 2011, eleven countries have been participating, which have revealed the emerging problem of antimicrobial resistance in this region. Similarly, in Africa, only 17% of member countries report data, which are mostly incomplete. Despite this, the region also confirms that antimicrobial resistance is a growing problem (5).

The list of global priority antibiotic-resistant bacteria, published by the WHO in 2017, for the research and development of new antibiotics, includes the following as critical priority: *Pseudomona*

aeruginosa and *Acinetobacter baumannii* resistant to carbapenems, as well as enterobacteria resistant to carbapenems and third-generation cephalosporins. The following are considered high priority: *Enterococcus faecium*, resistant to vancomycin; *S. aureus*, methicillin-resistant and resistant to vancomycin; *Helicobacter pylori*, resistant to clarithromycin; *Campylobacter* and *Salmonella* spp., resistant to fluoroquinolones; *Neisseria gonorrhoeae*, resistant to third-generation cephalosporins and fluoroquinolones. The following are of intermediate priority: *Streptococcus pneumoniae*, not susceptible to penicillin; *Haemophilus influenzae*, resistant to ampicillin, and *Shigella* spp., resistant to fluoroquinolones (6).

Nine of these bacteria, considered of great importance for public health, were included in the 2014 WHO report, with antimicrobial resistance data obtained from research articles, official reports, and surveillance networks in each WHO region (5). Thus, in all WHO regions, a percentage higher than 20% of methicillin-resistant *S. aureus* (MRSA) was reported. The highest percentage was found in the Americas (51.4%, range from 2.4 to 90%) and Africa (48%, range from 0 to 100%). The high proportions of MRSA imply an increased risk of infections and the need to use another group of antibiotics with lower selective toxicity, as well as the ease of dissemination of resistance among species of the genus *Staphylococcus*. *Streptococcus pneumoniae* resistant (or not susceptible) to penicillin was reported in 35% of the countries. However, it was detected in all WHO regions. The highest percentages were found in Africa (39.4%, range from 1 to 100%) and the Americas (33.4%, range from 0 to 53%).

Klebsiella pneumoniae isolates were reported by 41% of the member countries; in all, the percentage of resistance to third-generation cephalosporins was greater than 30%, and resistance to carbapenems exceeded 50% in some countries of Europe, Asia, and the Mediterranean. 45% of the member countries reported *E. coli* resistant to fluoroquinolones or to third-generation cephalosporins. The

highest percentage of isolates resistant to these antibiotics was reported in the regions of Africa, Asia, and the Mediterranean. The report also included other bacteria such as *Neisseria gonorrhoeae* with decreased susceptibility to cephalosporins, nontyphoidal *Salmonella*, and *Shigella* species resistant to fluoroquinolones.

In this way, the main programs from all over the world that implement the WHO global action plan are: Study for Monitoring Antimicrobial Resistance Trends (SMART), which provides data on gastrointestinal and urinary infections (7); the Sentry antimicrobial surveillance program, which monitors pathogens that cause nosocomial and community-acquired infections, as well as blood, respiratory tract, skin, soft tissue, and urinary tract infections; the study Tracking Resistance in the United States Today (TRUST) and the *Alexander* project monitor the antimicrobial susceptibility of *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis* as main agents of respiratory tract infections. These and other international programs, in addition to providing data on pathogen incidence and their resistance to antimicrobials, provide important information on the influence of antimicrobial use on resistance (8).

The surveillance and monitoring of antibiotic resistance in microorganisms isolated from ocular tissues has been carried out in two programs: TRUST and the Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR). The TRUST eye program started in 2005, and focused on three microorganisms: *S. aureus*, *Streptococcus pneumoniae*, and *Haemophilus influenzae*. The ARMOR study (Antibiotic Resistance Monitoring in Ocular Microorganisms) is a similar surveillance program created specifically to monitor ocular pathogens in the United States (9). The initial results of this study were published in 2011 (ARMOR 2009) (10), and subsequent data from 2009 to 2013 (ARMOR 2013) were published in 2017, with a total of 3237 isolates. It is the largest study of its kind to date (11).

Martín Algarra LV, Sánchez MC, Rondón Correa G, Rodríguez MF

The results of these three studies—ARMOR (2009, 2013) and TRUST—agree that the most prevalent microorganism was *S. aureus*, a high percentage of which was MRSA (39.0, 42.2, and 16.8%, respectively). Similarly, MRSA showed greater resistance to other antibiotics, such as macrolides, quinolones, and aminoglycosides, than methicillin-sensitive *S. aureus*. The percentage of *S. pneumoniae* not susceptible to penicillin was less than 20%, although it is important to bear in mind that these results depend on the cut-off points and methodologies used (9-11).

The bacteria that are part of the ocular microbiota, which is mainly composed of *coagulase-negative Staphylococcus* (CNS), have been considered opportunistic pathogens in recent years, as they have been reported as etiological agents of diseases, such as endophthalmitis, blepharitis, and conjunctivitis; with high prevalence and, in several cases, high resistance to antimicrobials (12-15) chocolate, and Sabouraud dextrose agar media. RESULTS: The mean age was 36.04 (SD 2.16. Other studies on the antimicrobial susceptibility of the ocular microbiota have evidenced that at least half of the CNS species (55.2%) show resistance to more than three antibiotics: penicillin (83%), oxacycline and erythromycin (49%), and fluoroquinolones (28%), the latter group frequently used in the treatment of ocular infections and as prophylactics in eye surgeries (16-18).

Bacterial infections of the conjunctiva are usually self-limiting. For this reason, microbiological identification or antimicrobial susceptibility and resistance testing are not carried out in most cases. However, topical antibiotics are formulated according to the patient's clinic, which are available over the counter in many countries. In this way, the antimicrobial resistance of bacteria isolated from infections or ocular microbiota is also associated with the duration and regularity of drug administration, which increases the rate of resistance to antimicrobial agents (19-21).

Resistance to antibiotics in microorganisms that cause systemic infections has been more closely monitored and published than resistance of microorganisms grown from ocular samples. For this reason, the objective of this research was to identify the main antimicrobial resistance profiles of bacteria isolated from infections or ocular microbiota, according to their geographical location, based on a literature review.

METHODOLOGY

An information search was carried out in EBSCOhost databases: Academic Search, Medline, ScienceDirect, Web of Science, Springer, PubMed, and Google Academic, with the following keywords: *ocular*, *antimicrobial*, and *resistance*, between 2010 and 2017. The strategy for the selection and analysis of the results published in studies was based on the following criteria:

1. Articles that report data related to antimicrobial resistance or susceptibility by genus or species of bacteria isolated from infections or ocular microbiota.
2. Articles that include a minimum of 40 samples or patients and analyze a minimum of 20 isolates.
3. Articles with moderate and high-quality evidence according to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) model.

The articles selected according to the first two criteria were typed into an Excel sheet, where they were differentiated by the country where the research was conducted, year of publication and study, type of study, sample size, total of bacterial isolates analyzed, genus and species of the bacteria reported, pathology and tissue in which bacteria were isolated, and the percentage of resistance to each antibiotic. The latter was calculated based on the total number of isolates when the article reported susceptibility, or it was subdivided into groups according to antimicrobial resistance phenotypes. To validate the information, two copies

of the same database were made by two of the researchers. Finally, to refine evidence quality, the following items were considered according to the GRADE scale, with some modifications:

- Sample randomization: insufficient or not done.
- Inconsistency of results: when the results showed wide variability or heterogeneity that was not explained.
- Uncertainty about the evidence: the results of antimicrobial after treatment intervention or follow-up were ruled out.
- Imprecision: based on whether or not confidence intervals (CI) were reported, studies that recorded susceptibility or resistance percentages only by group of microorganism were discarded.

RESULTS

30 articles were analyzed that contained data on etiological identification and antimicrobial resistance from the last seven years. In most countries, the genus *Staphylococcus* (*S. aureus*, 45%; CNS, 37%), *Pseudomonas* (8%), and *Streptococcus* (7%) predominated. *Corynebacterium* (2%) and *Klebsiella* (1%) showed the lowest percentages (Figure 1).

In the Americas, the highest percentage of isolates was of the genus *Staphylococcus*, obtained from eye infections and the ocular microbiota. The highest number of articles (ten) was found in the United States, and a total of 6335 isolates were reported (*S. aureus*, 2413; CNS, 1994; *Pseudomona*, 1090; *Streptococcus*, 768; *Klebsiella*, 70) (11,18,22-29)71 (67.6%. In Mexico, three articles were selected with a total of 392 isolates (*S. aureus*, 21; CNS, 278; *Streptococcus*, 12; *Corynebacterium*, 75; *Pseudomonas*, 6) (30-32). In Colombia, two articles were selected with 112 isolates (CNS, 82; *S. aureus*, 18; *Pseudomona*, 7; *Streptococcus*, 5) (15,33). From the other countries, only one article was selected, as follows: Cuba, with 1839 isolates (CNS, 965; *S. aureus*, 874) (34); Venezuela, with 168 isolates (CNS, 112; *S. aureus*, 56) (35); Brazil, with 33 isolates (CNS, 22; *S. aureus*, 11) (36), and Paraguay, with 22 isolates of *S. epidermidis* (37).
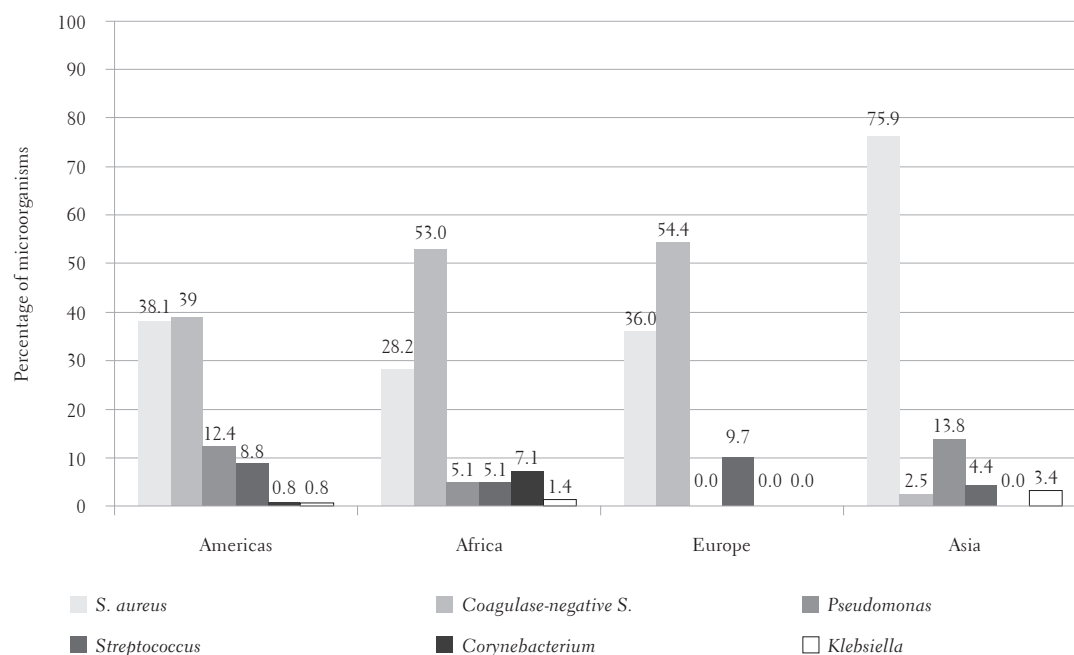

FIGURE 1. **Main microorganisms isolated from the eyeball by continent**

Martín Algarra LV, Sánchez MC, Rondón Correa G, Rodríguez MF

In Africa, the highest percentage of isolates were CNS reported in two articles from Ethiopia, with a total of 110 isolates (CNS, 60; *S. aureus*, 27; *Streptococcus*, 18; *Pseudomonas*, 3; *Klebsiella*, 2) (38,39); one article from Nigeria with 121 isolates (*S. aureus*, 43; CNS, 35; *Corynebacterium*, 25; *Pseudomonas*, 15; *Klebsiella*, 3) (40), and one article from Uganda with 120 isolates from the ocular microbiota (CNS, 91; *S. aureus*, 29) (41).

In Europe, CNS were the most identified in ocular infections. The largest number of isolates was obtained from an article that reported 635 (CNS, 313; *S. aureus*, 252; *Streptococcus pneumoniae*, 70) from medical centers in several European countries (France, Germany, Italy, Poland, Slovakia, Spain, and the United Kingdom) (42). Additionally, in Italy, an article was found with 20 isolates (CNS, 12; *S. aureus*, 8) (43), and in France, an article with 68 isolates of CNS from patients with endophthalmitis (44).

In Asia, the highest percentage of isolates published by two countries were of the genus *Pseudomonas*. In India, an article was found with 151 isolates (*Pseudomonas*, 75; CNS, 18; *S. aureus*, 20; *Klebsiella*, 24; *Streptococcus*, 14) (45), and in Pakistan, an article with 22 isolates of *P. aeruginosa* (46). In Nepal, the highest number of bacteria were *Streptococcus* (*Streptococcus*, 17; *S. aureus*, 1; *Pseudomonas*, 1) (47), and in Taiwan, in a retrospective study, 519 isolates of methicillin-resistant and methicillin-susceptible *S. aureus* were reported (48).

PERCENTAGES OF ANTIMICROBIAL RESISTANCE BY BACTERIA GENUS

S. aureus: In Europe and Asia, the highest percentage of resistance was found to beta-lactams (77.3 and 96.1%, respectively) and macrolides (54.9 and 33.9%, respectively). In the Americas, 59.5% of *S. aureus* was resistant to macrolides, and 33.8% to beta-lactams. Resistance to quinolones in Europe was in the third place of importance (45.0%), just like in America (20%). In Africa, the strains reported were mainly resistant to tetracyclines (52.6%) and to trimethoprim-sulfamethoxazole (33.0%) (Figure 2).
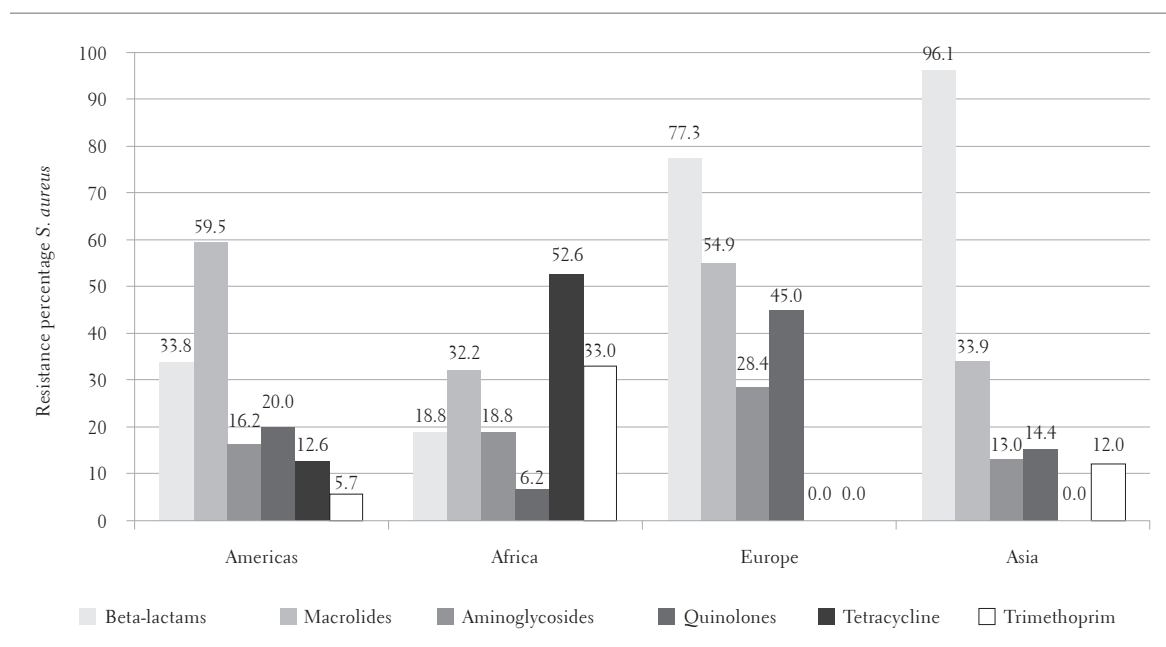

FIGURE 2. **Percentages of antimicrobial resistance of S. *aureus* per continent**

CNS: The highest percentage of antimicrobial resistance was to beta-lactams (82.0%) in Europe, and to macrolides in America (57.3%), Europe (46.7%), and Africa (19.5%). The highest resistance to quinolones was reported in the Americas (31.7%) and Europe (24.0%). Like S. *aureus*, the highest percentage of CNS strains resistant to tetracycline (32.8%) and to trimethoprim-sulfamethoxazole (33.0%) was found in Africa. The highest resistance to aminoglycosides was found in Europe (31.4%) (Figure 3).

Pseudomonas: Beta-lactams were the main group of antibiotics to which this microorganism showed resistance in Asia and the Americas (70.8 and 42.4%, respectively). Resistance to tetracyclines was the highest in Asia (59.0%) and Africa (33.3%); high resistance to quinolones (36.7%), aminoglycosides (35.5%), and trimethoprim-sulfamethoxazole (33.0%) was also reported on this continent (Figure 4).

Streptococcus: The antibiotics to which *Streptococcus* showed the greatest resistance were tetracyclines (59%) in Africa, and macrolides in the Americas (40.0%) and Europe (27.0%). Resistance to beta-lactams was reported in Africa (23.8%) and the Americas (15.9%) (Figure 5).

Corynebacterium isolates were only found in reports from the countries of the Americas and Africa, where this microorganism showed the greatest resistance to clindamycin (60%) and to chloramphenicol (24%), respectively. A significant percentage showed resistance to beta-lactams in both continents (25%). Finally, *Klebsiella* reports were only found in the Americas and Africa, where the greatest resistance was to chloramphenicol (67%) and tetracyclines (50%); they also showed resistance to beta-lactams (28%) and aminoglycosides (12%).
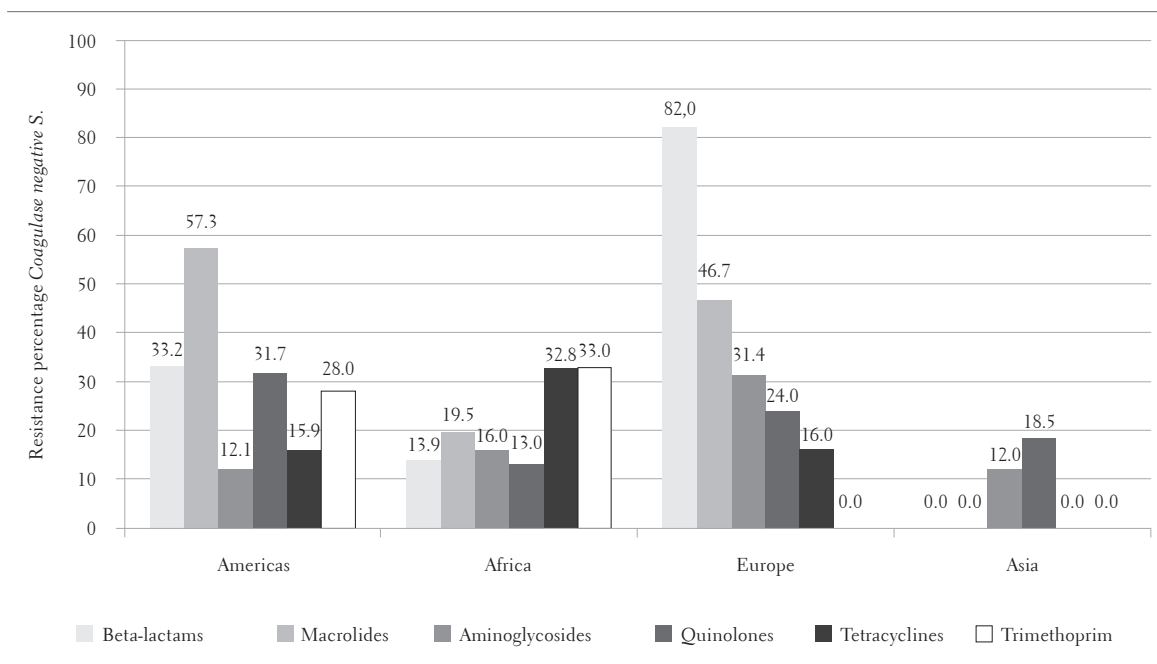

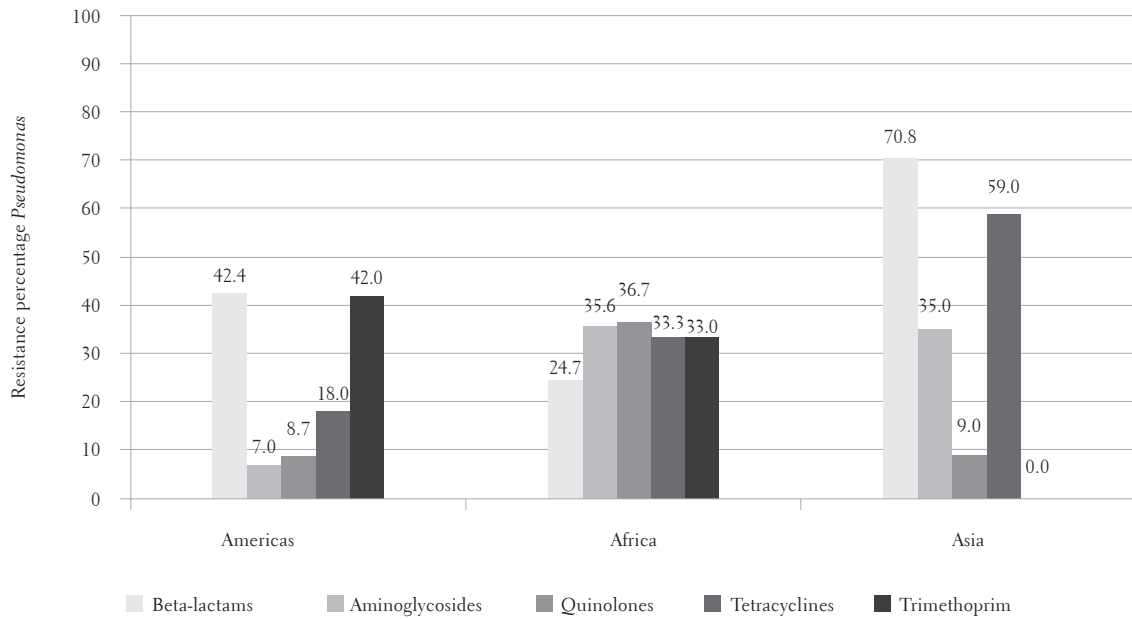**FIGURE 3. Percentage of antimicrobial resistance of CNS per continent**

Martín Algarra LV, Sánchez MC, Rondón Correa G, Rodríguez MF

FIGURE 4. **Percentages of antimicrobial resistance of *Pseudomonas* by continent**
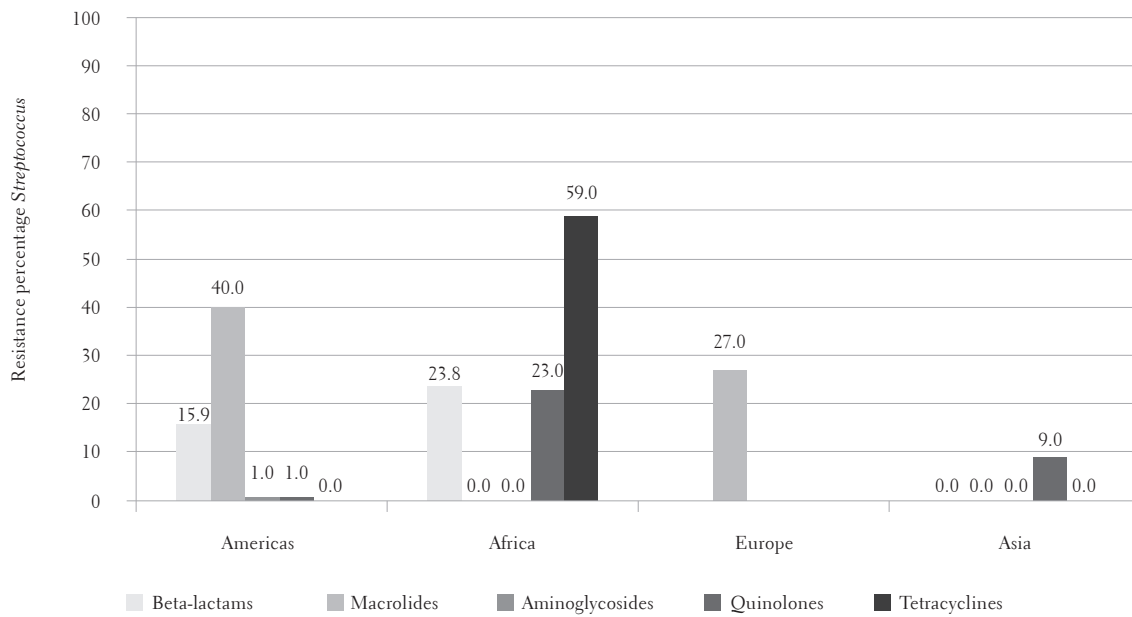

FIGURE 5. **Percentages of antimicrobial resistance of *Streptococcus* per continent**

DISCUSSION

Beta-lactam antibiotics represent the largest group of antimicrobials and are frequently used as therapeutic agents in bacterial infections (49). Resistance to penicillin was identified for the first time by Abraham and Chain in 1940, in strains of *E. coli* that produced penicillinases or beta-lactamases (50). Subsequently, it was identified that *Staphylococcus* species had the same resistance mechanism, which is transferred horizontally between them. This bacterium also develops

resistance to almost all beta-lactams, thanks to the acquisition of the mecA gene, which modifies the target (transpeptidases or PBP). This gene is located in the *Staphylococcal* chromosomal cassette (SCC), which corresponds to a mobile element (genomic island) for gene exchange. So far, five types of SCC*mec* have been identified (I, II, III, IV, V), according to the combination of the *ccr* and *mec* complexes (51). *ccr* genes code for recombinases, specific sites where SCC is integrated into the chromosome and the *mec* complex, which include the *mec*R1 and *mec*I regulatory genes and insertion sequences (IS), responsible for connecting and grouping other resistance genes. The present review found that 57% of ocular isolates reported in the world show resistance to beta-lactams. Making a parallel to hospital infections, approximately 90% of *Staphylococcus* strains are resistant to the group of beta-lactam antibiotics (mainly penicillins); therefore, increase in resistance to these antibiotics implies a serious therapeutic problem in the hospital setting (52,53).

For two decades, *S. aureus* has been the most predominant agent in bloodstream, skin, soft tissue, and respiratory tract infections around the world. Similarly, it was found that in infections and in the ocular microbiota, this genus is the most reported in almost all selected publications, which is consistent with its great ability to accumulate virulence and antimicrobial resistance genes. Data from the Sentry antimicrobial resistance monitoring program between 1997 and 1999 revealed that the highest percentage of MRSA was found in Asia (> 50%), the Americas (> 30%), and Europe (> 28%), and that the percentage of methicillin-resistant CNS exceeded 70% in all continents (54).

In this review, the highest percentages of resistance to beta-lactams were found in Europe (> 75%) and Asia (> 96%). The most commonly reported beta-lactam antibiotics were penicillin, amoxicillin-sulbactam, oxacillin, and ceftriazone. Since oxacillin resistance has not been genotypically confirmed in most of these studies, the results of this investigation differ mainly because these

percentages include resistance to all beta-lactams and not only to methicillin, as reported in the global reports. It is possible that this has contributed to the higher proportions of resistance to beta-lactams found in ocular isolates.

Given that in clinical practice these antibiotics are not widely used for the local treatment of eye infections, it is possible that systemic use directly influences their resistance. In fact, the global TRUST and ARMOR reports indicate high percentages of MRSA and methicillin-resistant CNS in ocular isolates (10,55). In addition, consistent with these global reports, many strains showed resistance to other groups of antibiotics, especially to macrolides (azithromycin and erythromycin), which are widely used in the local context in almost all countries for the treatment of eye infections. Resistance to quinolones was found in a higher percentage in *S. aureus* and CNS reported in Europe and the Americas.

The resistance of *Streptococcus* isolates depended on the geographical location. In Africa, the greatest resistance was to tetracyclines, and in the Americas and Europe, to macrolides. However, the number of isolates in the selected publications was very low (< 10%), so these reports cannot be compared with global reports on the resistance of this bacterium. Similarly, *Pseudomonas* isolates accounted for less than 15%, and no publications were found in Europe. However, a relatively high percentage was found in all three continents for almost all antibiotics, especially in Africa. It is possible that this indicates the existence of multidrug-resistant strains, a growing problem in this genus in the entire world (24).

The results reported in the articles have shown that the antimicrobial resistance of ocular pathogens has increased in recent years. This is due to an inadequate use of systemic and topical antibiotics for infections that are not bacterial (viral), incorrect medication dosage, and excessive treatment duration. Such factors contribute to the antimicrobial resistance of pathogens in the eye zone and hinder

Martín Algarra LV, Sánchez MC, Rondón Correa G, Rodríguez MF

the adequate management of infections (56). For this reason, it is essential to make an adequate identification of the etiological agent of the infection and its susceptibility profile (57), in order to confirm the diagnosis, provide timely treatment based on therapeutic decisions that are aimed at eliminating the specific pathogen, and avoid the formation of bacteria resistant to antibiotics.

Finally, the authors acknowledge that the main limitation in this review was the lack of data. In most of the countries, only one publication was found, and in some of the studies, the selection and size of the sample was not randomized or representative. Despite this, the present study highlights the importance of improving knowledge about the antimicrobial resistance of bacteria isolated from infections and the ocular microbiota, which, fortunately, has been promoted in recent years in countries such as the United States, with the support of WHO.

REFERENCES

1. World Health Organization. Worldwide country situation analysis: response to antimicrobial resistance [internet]. Ginebra: WHO Press; 2015 [cited 2018 Jan. 21]. p. 1-50. Available from: http://www.who.int/drugresistance/documents/situationanalysis/en/

2. World Health Organization, Pan American Health Organization, Robert Stempel College of Public Health & Social Work. Monitoring and Evaluation of the Global Action Plan on Antimicrobial Resistance (AMR): Regional Expert Consultation on Monitoring and Evaluation of AMR Interventions. Washington, DC; 2017.

3. Laxminarayan R, Duse A, Wattal C, Zaidi AKM, Wertheim HFL, Sumpradit N, et al. The Lancet Infectious Diseases Commission Antibiotic resistance—The need for global solutions. Lancet Infect Dis. 2013;3099(13):1-42.

4. Food and Drug Administration. Consumer updates-Combating antibiotic resistance [internet]. Office of the Commissioner; 2011 [cited 2018 Apr 18]. Available from: https://www.fda.gov/forconsumers/consumerupdates/ucm092810.htm

5. World Health Organization. Antimicrobial resistance. Reporte global on surveillance [internet]. Bulletin of the World Health Organization [cited 2018 Mar 22]. 2014;61. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22247201%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2536104&tool=pmcentrez&rendertype=abstract

6. Tacconelli E, Harbarth S, Kahlmeter G, Kluytmans J, Mendelson M, Hospital GS, et al. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. Ginebra: World Health Organization; 2017.

7. Morrissey I, Hackel M, Badal R, Bouchillon S, Hawser S, Biedenbach D. A review of ten years of the Study for Monitoring Antimicrobial Resistance Trends (SMART) from 2002 to 2011. Pharmaceuticals. 2013;6(11):1335-46.

8. Masterton R. The importance and future of antimicrobial surveillance studies. Clin Infect Dis. 2008;47(S1):S21-31.

9. Asbell PA, Colby KA, Deng S, McDonnell P, Meisler DM, Raizman MB, et al. Ocular TRUST: nationwide antimicrobial susceptibility patterns in ocular isolates. Am J Ophthalmol. 2008;145(6):957-8.

10. Haas W, Pillar CM, Torres M, Morris TW, Sahm DF. Monitoring antibiotic resistance in ocular microorganisms: Results from the Antibiotic Resistance Monitoring in Ocular Microrganisms (ARMOR) 2009 surveillance study. Am J Ophthalmol. 2011;152(4):567-74.

11. Asbell PA, Sanfilippo CM, Pillar CM, DeCory HH, Sahm DF, Morris TW. Antibiotic resistance among ocular pathogens in the United States five-year results from the Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR) surveillance study. JAMA Ophthalmol. 2015;133(12):1445-54.

12. Gündüz A, Gündüz A, Cumurcu T, Seyrek A. Conjunctival flora in Behçet patients. Can J Ophthalmol. 2008;43(4):476-9.

13. Hernández P, Quintero G. Etiología bacteriana de infecciones oculares externas. Nova. 2003;1(1):57-64.

14. Bharathi MJ, Ramakrishnan R, Shivakumar C, Meenakshi R, Lionalraj D. Etiology and antibacterial susceptibility pattern of community-acquired bacterial ocular infections in a tertiary eye care hospital in south India. Indian J Ophthalmol. 2010;58(6):497-507.

15. Hernandez-Rodríguez P, Quintero G, Mesa D, Molano R, Hurtado P. Prevalencia de Staphylococcus epidermidis y Staphylococcus aureus en pacientes con conjuntivitis. Univ Sci. 2005;10(2):47-54.

16. Ta CN, Chang RT, Singh K, Egbert PR, Shriver EM, Blumenkranz MS, Miño de Kaspar H. Antibiotic resistance patterns of ocular bacterial flora. Ophthalmology. 2003;110(10):1946-51.

17. Kim SJ, Toma HS. Antimicrobial resistance and ophthalmic antibiotics. Arch Ophthalmol. 2011;129(9):1180-8.

18. Hsu HY, Lind JT, Tseng L, Miller D. Ocular flora and their antibiotic resistance patterns in the midwest:

A prospective study of patients undergoing cataract surgery. Am J Ophthalmol. 2013;155(1):36-44.

19. Avorn JL, Barrett JF, Davey PG, McEwen SA, O'Brien TF, Levy SB. Antibiotic resistance: synthesis of recommendations by expert policy groups. Génova: World Health Organization; 2001.

20. French GL. Clinical impact and relevance of antibiotic resistance. Adv Drug Deliv Rev. 2005;57(10):1514-27.

21. Leeming JP. Treatment of ocular infections with topical antibacterials. Clin Pharmacokinet. 1999;37(5):351-60.

22. Chung JL, Seo KY, Yong DE, Mah FS, Kim T, Kim EK, et al. Antibiotic susceptibility of conjunctival bacterial isolates from refractive surgery patients. Ophthalmology. 2009;116(6):1067-74.

23. Miller D. Update on the epidemiology and antibiotic resistance of ocular infections. Middle East Afr J Ophthalmol. 2017;24(1):30-42.

24. Kim SJ, Toma HS, Midha NK, Cherney EF, Recchia FM, Doherty TJ. Antibiotic resistance of conjunctiva and nasopharynx evaluation study: a prospective study of patients undergoing intravitreal injections. Ophthalmology. 2010;117(12):2372-8.

25. Hsu J, Gerstenblith AT, Garg SJ, Vander JF. Conjunctival flora antibiotic resistance patterns after serial intravitreal injections without postinjection topical antibiotics. Am J Ophthalmol. 2014;157(3):514-8.

26. Alabiad CR, Miller D, Schiffman JC, Davis JL. Antimicrobial resistance profiles of ocular and nasal flora in patients undergoing intravitreal injections. Am J Ophthalmol. 2011;152(6):999-1004.

27. Kim SJ, Toma HS. Ophthalmic antibiotics and antimicrobial resistance. Ophthalmology. 2011;118(7):1358-63.

28. Dave SB, Toma HS, Kim SJ. Ophthalmic antibiotic use and multidrug-resistant staphylococcus epidermidis. Ophthalmology. 2011;118(10):2035-40.

29. Major JC, Engelbert M, Flynn HW, Miller D, Smiddy WE, Davis JL. Staphylococcus aureus endophthalmitis: antibiotic susceptibilities, methicillin resistance, and clinical outcomes. Am J Ophthalmol. 2010;149(2):278-83.

30. Olivares-Medina RM, Ángeles-Martínez E, Ortega-Larrocea G, León-Hernández RR, Juárez-Hernández RI, Tellez-Gastelum RM, et al. Flora bacteriana conjuntival preoperatoria. Rev Mex Oftalmol. 2009;83(5):267-71.

31. Chirinos-Saldaña P, Graue-Hernández EO, Hernández-Camarena JC, Navas A, Ramírez-Miranda A, de León LRD, et al. Perfil microbiológico y sensibilidad a antibióticos de microorganismos aislados de infecciones conjuntivales en el Instituto de Oftalmología Fundación Conde de Valenciana. Reporte del año 2012. Rev Mex Oftalmol. 2014;88(2):73-7.

32. Hernández-Camarena JC, Bautista-de Lucio VM, Chirinos-Saldaña P, Navas A, Ramírez-Miranda A, Climent-Flores A, et al. Queratitis infecciosas: tendencias microbiológicas y sensibilidad a antibióticos. Segundo reporte anual del grupo de Estudio de Microbiología Ocular del Instituto de Oftalmología "Conde de Valenciana". Rev Mex Oftalmol. 2013;87(2):100-9.

33. Galvis V, Tello A, Guerra A, Acuña MF, Villarreal D, Villarreal D. Sensibilidad antibiótica de bacterias obtenidas de queratitis e infecciones intraoculares en la Fundación Oftalmológica de Santander (FOSCAL), Floridablanca, Colombia. Biomédica. 2014;34(Supl. 1):23-33.

34. Noya Cabaña A, Llamos Durive R, Rodríguez Acosta C, Rojas Hernández N, Castro Sánchez N, Méndez Duque de Estrada A. Incidencia y fármaco-resistencia de cepas de Staphylococcus spp. aisladas de exudados conjuntivales. Rev Cuba Oftalmol. 2010;23(supl. 1):568-79.

35. Rodríguez LA, Porras DJ, Villegas AE, Molina J. Susceptibilidad in vitro de la flora bacteriana ocular preoperatoria a 4 fluoroquinolonas. Vitae. 2013;(43):1-8.

36. Endriss D, Brandt CT, de Castro CMMB, Oliveira VF, de Fátima Alves Diniz M. Microbiota conjuntival e resistência a antibióticos em recém-nascidos prematuros internados em unidade de terapia intensiva. Arq Bras Oftalmol. 2009;72(3):291-5.

37. Fariña N, Samudio M, Carpinelli L, Nentwich MM, de Kaspar HM. Methicillin resistance and biofilm production of Staphylococcus epidermidis isolates from infectious and normal flora conjunctiva. Int Ophthalmol. 2017;37(4):819-25.

38. Assefa Y, Moges F, Endris M, Zereay B, Amare B, Bekele D, et al. Bacteriological profile and drug susceptibility patterns in dacryocystitis patients attending Gondar University Teaching Hospital, Northwest Ethiopia. BMC Ophthalmol. 2015;15:34.

39. Shiferaw B, Gelaw B, Assefa A, Assefa Y, Addis Z. Bacterial isolates and their antimicrobial susceptibility pattern among patients with external ocular infections at Borumeda hospital, Northeast Ethiopia. BMC Ophthalmol. 2015;15:103.

40. Iwalokun BA, Oluwadun A, Akinsinde KA, Niemogha MT, Nwaokorie FO. Bacteriologic and plasmid analysis of etiologic agents of conjunctivitis in Lagos, Nigeria. J Ophthalmic Inflamm Infect. 2011;1(3):95-103.

41. Mshangila B, Paddy M, Kajumbula H, Ateenyi-Agaba C, Kahwa B, Seni J. External ocular surface bacterial isolates and their antimicrobial susceptibility patterns among pre-operative cataract patients at Mulago National Hospital in Kampala, Uganda. BMC Ophthalmol. 2013;13(1):71.

42. Sanfilippo CM, Morrissey I, Janes R, Morris TW. Surveillance of the activity of aminoglycosides and fluoroquinolones against ophthalmic pathogens from Europe in 2010-2011. Curr Eye Res. 2016;41(5):581-9.

43. Blanco AR, Sudano Roccaro A, Spoto CG, Papa V. Susceptibility of methicillin-resistant Staphylococci

Antimicrobial resistance profile of bacteria isolated from infections an the ocular microbiota

ARTÍCULOS DE INVESTIGACIÓN CIENTÍFICA Y TECNOLÓGICA

clinical isolates to netilmicin and other antibiotics commonly used in ophthalmic therapy. Curr Eye Res. 2013;38(8):811-6.

44. Chiquet C, Maurin M, Altayrac J, Aptel F, Boisset S, Vandenesch F, et al. Correlation between clinical data and antibiotic resistance in coagulase-negative Staphylococcus species isolated from 68 patients with acute post-cataract endophthalmitis. Clin Microbiol Infect. 2015;21(6):592.e1–592.e8.

45. Reddy AK, Reddy RR, Paruvelli MR, Ambatipudi S, Rani A, Lodhi SAK, et al. Susceptibility of bacterial isolates to vancomycin and ceftazidime from patients with endophthalmitis: Is there a need to change the empirical therapy in suspected bacterial endophthalmitis? Int Ophthalmol. 2015;35(1):37-42.

46. Abidi SH, Sherwani SK, Siddiqui TR, Bashir A, Kazmi SU. Drug resistance profile and biofilm forming potential of Pseudomonas aeruginosa isolated from contact lenses in Karachi-Pakistan. BMC Ophthalmol. 2013;13(1):57.

47. Suwal S, Bhandari D, Thapa P, Shrestha MK, Amatya J. Microbiological profile of corneal ulcer cases diagnosed in a tertiary care ophthalmological institute in Nepal. BMC Ophthalmol. 2016;16(1):209.

48. Chuang C-CC, Hsiao C-HH, Tan H-YY, Ma DH-KK, Lin K-KK, Chang C-JJ, et al. Staphylococcus aureus ocular infection: methicillin-resistance, clinical features, and antibiotic susceptibilities. PLoS One. 2012;7(8):1-7.

49. Morejón García M. Betalactamasas de espectro extendido. Rev Cubana Med. 2013;52(4):272-80.

50. Abraham EP, Chain E. An enzyme from bacteria able to destroy penicillin. Nature. 1940;146(3713):837.

51. Hanssen AM, Ericson Sollid JU. SCCmec in staphylococci: genes on the move. FEMS Immunol Med Microbiol. 2006;46(1):8-20.

52. Torres I. Estudio de la resistencia de Staphylococcus aureus meticilino resistente (MRSA) e identificación del gen mecA por reacción en cadena de la polimerasa en tiempo real empleando el equipo: GeneXpert Cepheid [thesis]. Toluca: Universidad Autónoma del Estado de México; 2014.

53. Secretaría Distrital de Salud de Bogotá D. C. Política de prevención, control y vigilancia epidemiológica de infecciones intrahospitalarias (IIH) para Bogotá, D. C. [internet]. Bogotá; 2007 [cited 2018 May 22]. Available from: http://www.saludcapital.gov.co/Polticas%20en%20Resolucin/POLITICA%20DE%20PREVENCION,%20VIGILANCIA%20DE%20INFECCIONES%20INTRAHOSPITALARIAS.pdf

54. Diekema, DJ, Pfaller M, Schmitz J, Smayevsky J, Bell J, Jones N, et al. Survey of infections due to Staphylococcus species: frequency of occurrence and antimicrobial susceptibility of isolates collected in the United States, Canada, Latin America, Europe and the Western Pacific Region for the Sentry Antimicrobial Surveillance, 1997-1999. Clin Infect Dis. 2001;15(supl. 2):S114-32.

55. Asbell PA, Sanfilippo CM, Pillar CM, DeCory HH, Sahm DF, Morris TW. Antibiotic resistance among ocular pathogens in the United States: five-year results from the Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR) surveillance study. JAMA Ophthalmol. 2015;133(12):1445-54.

56. Sharma S. Antibiotic resistance in ocular bacterial pathogens. Indian J Med Microbiol. 2011;29(3):218-23.

57. Kowalski R. Is antibiotic resistance a major problem in ophthalmology? Acta Ophthalmol [Internet]. 2012;90(s249). doi: https://doi.org/10.1111/j.1755-3768.2012.3444.x